



UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
-----------------	-------------	----------------------	---------------------	------------------

10/589,718

08/16/2006

Bo-Lennart Johansson

PU0406

8796

22840 7590 11/13/2007
GE HEALTHCARE BIO-SCIENCES CORP.
PATENT DEPARTMENT
800 CENTENNIAL AVENUE
PISCATAWAY, NJ 08855

EXAMINER

SAUNDERS, DAVID A

ART UNIT

PAPER NUMBER

1644

MAIL DATE

DELIVERY MODE

11/13/2007

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary

Application No.

10/589,718

Applicant(s)

JOHANSSON ET AL.

Examiner

David A. Saunders

Art Unit

1644

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 03 May 2007.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-12 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-12 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date _____.
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____.
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: _____.

AMENDMENT ENTRY

The Preliminary Amendment of 8/16/06 has been entered. The claims presented in the paper filed on 5/3/07 are deemed to be merely a copy of the original Claims and not an amended version of the claims (See p 2 of Petition filed on 5/3/07). Claims 1-12 are pending. Claims 1-12 are under consideration.

OBJECTION(S) TO DISCLOSURE

The disclosure is objected to because of the following informalities:

While the petition filed 5/3/07, to accept color photographs and color drawings, presented three (3) color copies of the drawings, the attached specification was not presented as an amended version of the originally filed specification. Thus the specification is considered to be that originally filed on 8/16/06. The specification is objected to for failing to contain the required following language as the first paragraph of the brief description of the drawings section of the specification:

The patent or application file contains at least one drawing executed in color. Copies of this patent or patent application publication with color drawing(s) will be provided by the Office upon request and payment of the necessary fee.

Appropriate correction is required. Applicant is reminded of the proper procedure for amending the specification set forth in 37 CFR 1.121. Only the paragraph to be inserted may be submitted, with unambiguous instructions as to where to insert it.

It is further noted that, even though applicant has referred "another copy of the thirty-nine (39) page specification as filed" (See p 2 of Petition filed on 5/3/07), the "copy" of the specification filed on 5/3/07 is not a copy of the original specification. If this

Art Unit: 1644

"copy" had been presented as a substitute specification, it would have been objected to under 35 U.S.C. 132(a) because it introduces new matter into the disclosure. 35 U.S.C. 132(a) states that no amendment shall introduce new matter into the disclosure of the invention. The added material which is not supported by the original disclosure is the incorporation by reference of PCT and Swedish applications at page 1. Such incorporation by reference of the Swedish priority application was not recited in the originally filed PCT application and, hence, would constitute new matter. The incorporation by reference of the PCT application is pointless, since the instant application is the national stage of the PCT application.

Any formal amendment to the specification that incorporates the Swedish priority application by reference will be objected to under 35 USC 132(a).

OBJECTION(S) TO CLAIMS

Claims 9 and 11 are objected to under 37 CFR 1.75(i), as being of improper dependent form for failing to indent each component of the kit or system. Applicant is required to place the claim(s) in proper form. Furthermore, applicant is required to recite any modifying "wherein" clauses in the same paragraph as that listing the component being described in the wherein clause. Any such "wherein" clause must not appear as a separate paragraph at the end of the claim.

REJECTION(S) UNDER 35 USC 112, SECOND PARAGRAPH

Claims 2-6 and 9-12 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In claims 2 and 10, "the aromatic or heteroaromatic entity" lacks antecedent basis, since no "entity" has been recited in base claims 1 or 9.

In claims 2 and 10, it is not clear what "selected from the group consisting of C, S or O" is referring to. An "aromatic or heteroaromatic entity" inherently contains "C"; thus, why is applicant bothering to list "C" after "selected from"? Any "aromatic" ring system would only contain "C"; thus why is applicant further defining the "aromatic" ring system by reciting that the ring atoms are "selected from the group consisting of C, S or O"?

In claim 4, "the solution applied to" lacks antecedent basis, because base claim 1 has recited "contacting" rather than "applying" a solution.

In each of claims 4 and 6, "the multi-modal chromatography resin" lacks antecedent basis, because claim 1 has recited a "multi-modal ligand" rather than a "multi-modal chromatography resin".

Regarding claim 4, the phrase "and preferably" renders the claim indefinite because it is unclear whether the limitations following the phrase are part of the claimed invention. See MPEP § 2173.05(d).

Claim 9 is rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential structural cooperative relationships of elements, such omission

amounting to a gap between the necessary structural connections. See MPEP

§ 2172.01. The omitted structural cooperative relationships are: in the recitation of “wherein a multi-modal ligand...”, at the last 2 lines of claim 9, there is a lack of any nexus to the other kit components, because nothing therein positively states that this “multi-modal ligand” is on the “multi-modal chromatography resin”, recited at line 2.

Furthermore, any limitations that set forth the nature of any “ligand” on the “chromatography resin” must be inserted where the “chromatography resin” is listed as a kit component, rather than at the end of the claim.

Claims 11-12 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential structural cooperative relationships of elements, such omission amounting to a gap between the necessary structural connections. See MPEP § 2172.01. The omitted structural cooperative relationships are: there is no nexus between the “means for pumping” and the other recited components – e.g. is the “means for pumping” associated with the “means for adding”, is it between the first and second column”? There is no nexus between the “valving” and the other recited components – e.g. is the “valving” associated with the “means for adding”, is it between the first and second column”, is it after the second column? Dependent claim 12 provides no nexus between what is “automated” and the components listed in base claim 11 – e.g. is it the “means for adding”, the “means for pumping”, the “valving”, or all of these that is(are) “automated”?

Art Unit: 1644

EFFECTIVE FILING DATE OF THE CLAIMS

Prior to citing art, it is necessary to determine the effective filing date of the claims. Instant claim(s) 12 recites one or more feature(s) not disclosed in the Swedish priority application. Therefore the effective filing date for claim 12 is that of PCT/SE05/00292, filed on 2/24/05.

REJECTION(S) UNDER 35 USC 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1-3 and 6-8 are rejected under 35 U.S.C. 102(b) as being anticipated by Lihme et al (6,498,236), cited on 1449).

Lihme et al teach a chromatography resin having a multi-modal ligand, which comprises a mono- or bicyclic aromatic or heteroaromatic ligand and an acidic substituent, such as a carboxylic acid. See abstract; see col. 5, lines 25-67; col. 15, lines 25-41. The carboxylic acid substituent would serve as a weak cation exchanger, in

Art Unit: 1644

accord with instant claim 3, in view of the fact that applicant's own disclosure teaches that a carboxylic acid group can serve as a weak cation exchanger. Though Lihme et al do not verbatim teach that the carboxylic group serves as a weak cation exchanger, such is what the carboxylic acid group inherently is. The nature of the mono- or bicyclic aromatic or hetero aromatic ligand is disclosed at col. 13, line 19-col. 14, line 67. Numerous of these have structures consistent with the limitations of instant claim 2. As such, the affinity ligands of Lihme et al are multi-modal".

Lihme et al teach the instant contacting step. See the abstract; see, for example, col. 5, lines 54-60; col. 6, lines 35-52. The contacting step adsorbs immunoglobulin/antibody to the resin. Some contaminants wash through the column, while other contaminants adsorb to the column, in accord with instant claim 6. Adsorbed immunoglobulin/antibody and contaminants are then differentially eluted from the resin, in accord with instant claim 7. See, for example, col. 6, line 54-col. 7, line 57. The immunoglobulin/antibody being purified can be from a variety of sources; see col. 8, lines 7-24; col. 9, line 18- col. 10, line 32.

Regarding claim 8, Lihme et al teach purification of monoclonal antibodies from hybridoma cell cultures (e.g. col. 1, lines 30-34; col. 9, lines 18-26).

Numerous portions of applicant's disclosure have pointed to distinctions between the instant invention and Pat. 6,498,236 of Lihme et al. However, these distinctions pertain to features which are not recited in the instant claim limitations.

Claims 1-3 and 7 are rejected under 35 U.S.C. 102(b) or (e) as anticipated by Belew et al (US 6,852,230 or WO 02/053288, cited on 892).

WO 02/053288 has 102(b) date, as of its publication date of 7/11/02, since it was published more than one year prior to applicant's Swedish priority date of 2//27/04. US 6,852,230 has a 102(e) date of 6/19/03.filing date, since it is published in English and designates the US. For convenience the examiner will only refer to US 6,117,996 by col. and line numbers.

Belew et al teach multi-modal affinity ligands containing an aromatic or heteroaromatic ring and a carboxylic acid group, as a weak cation exchange group. Proteins such as BSA or IgG can be adsorbed thereto and then eluted therefrom. See the ligands listed in Table I, with the absorbance maximum and recovery percentages indicated. Johansson et al teach that such multi-modal affinity ligands can be used in desalting processes; the "contaminants" recited in instant claim 1 can be properly considered as encompassing salts. Thus instant claims 1, 3 and 7 are anticipated.

Regarding claim 2, the structures shown by Belew et al for ligands 1-7 and 9-11, in Table 1 have ring atoms that meet the limitations of claim 2.

REJECTION(S) UNDER 35 USC 102/103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1, 3 and 7-8 are rejected under 35 U.S.C. 102(b) as being anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Lowe et al (US 6,117,996, cited on Form 892, or WO 97/10887, cited on Form 1449).

US 6,117,996 and WO 97/10887 have the same disclosure. For convenience the examiner will only refer to US 6,117,996 by col. and line numbers.

Lowe et al ('996) teach a matrix having affinity ligands with a heteroaromatic ring, and substituents R1 and R4-R6 added thereto. These substituents can include an acidic group, such as a carboxylic group (COOH). See col. 4, lines 25 and 41; col. 7, lines 23 and 40. See, also preferred structures iv), vi) and viii) at cols. 11-12 and in claim 24. A carboxylic acid group would act as a weak cation exchanger, in accord with instant claim 3, in view of the fact that applicant's own disclosure teaches that a carboxylic acid group can serve as a weak cation exchanger. Though Lowe et al do not verbatim teach that the carboxylic group serves as a weak cation exchanger, such is what the

Art Unit: 1644

carboxylic acid group inherently is. Thus the affinity ligands of Lowe et al are "multi-modal".

Lowe et al teach that a matrix having the taught affinity ligands can be used to specifically adsorb an immunoglobulin thereto, in the same manner that Protein A or Protein G have been used as affinity ligands (col. 3, lines 41-65). Claims 1 and 3 are thus anticipated or, at the least, would have been obvious, in the event that applicant considers that the carboxylic acid group is merely taught as one of many choices.

Regarding claim 7, Lowe et al teach that the contacting/applying step adsorbs immunoglobulin/ antibody to the resin. Adsorbed immunoglobulin/antibody is then eluted/desorbed from the resin; see col. 20, lines 21-29.

Regarding claim 8, Lowe et al teach purification of monoclonal antibodies at col. 1, lines 54-65. Also, any of the engineered immunoglobulins produced by an engineered cell line (e.g. col. 14, lines 63-65) would inherently be "monoclonal".

Claims 1-3 and 7 are rejected under 35 U.S.C. 102(a) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Johansson et al (Jour. Chromat. A, 1016, 35, 2003, cited on 1449).

Johansson et al teach multi-modal affinity ligands containing an aromatic or heteroaromatic ring and a carboxylic acid group, as a weak cation exchange group. Proteins such as BSA, human IgG, or lysozyme can be adsorbed thereto and then eluted therefrom. Johansson et al teach that such multi-modal affinity ligands can be used in purification processes (pages 36 and 48). As such, instant claims 1, 3 and 7

are anticipated. In the event that applicant considers the teachings at pages 36 and 48 to be merely suggestive, obviousness is stated as an alternative rejection.

Regarding claim 2, the structures shown by Johansson et al for ligands 2, 4, 5, 8, for ligands 3, 6, 10, for ligand 7, for ligands 11, 17, and for ligand 15 (see Fig. 3) have ring atoms that meet the limitations of claim 2.

REJECTION(S) UNDER 35 USC 103

Claims 1-3 and 7 are rejected under 35 U.S.C. 103(a) as obvious over Maloisel et al (WO 03/024588, cited on Form 1449).

WO 03/024588 has 102(a) date, as of its publication date, since it was published within one year prior to applicant's Swedish priority date of 2//27/04. WO 03/024588 has a 102(e) date, as of its filing date, since it is published in English and designates the US.

Maloisel et al (WO 03/024588) teach mixed-mode/multimodal affinity ligands for cation exchange chromatography. Numerous of the ligands shown in Tables 1A (pp 35-36) and 1B (p 40) and Table 2 (p 44) have an aromatic or heteroaromatic ring and a carboxyl group, as a weak cation exchange group. Numerous of these aromatic or heteroaromatic rings have a structure consistent with the limits of instant claim 2. Johansson et al teach that such multi-modal affinity ligands can be used in purification processes (pages 20-23). Proteins such as Cyt-C, BSA, human IgG, or lysozyme can be adsorbed thereto (Examples 12-14). While they do not actually exemplify desorption/recovery of the matrix bound proteins (Example 14), it is taken that they

Art Unit: 1644

provide sufficient direction for one of skill in the art (pages 21-23) for one to accomplish desorption/recovery/elution of an IgG that has been bound to the matrix, without undue experimentation. Thus instant claims 1-3 and 7 would have been obvious.

Claims 9-10 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lihme et al, Belew et al, Johansson et al, or Maloisel et al, any in view of Hunt et al (US 2002/0110495, cited on Form 892).

Each of the Lihme et al, Belew et al, Johansson et al, and Maloisel et al references have been cited supra, against claims 1-3, for showing chromatographic separation of antibodies/immunoglobulins on a multi-modal chromatography medium/matrix/resin, which is consistent with that recited in both of instant claims 1 and 9. Hunt et al show that it was known to provide a chromatography medium/matrix/resin, in a kit, along with buffers. The chromatography medium/matrix/resin provided in the kit can be any one of a variety of types, including ion exchange resins. Since each of the primary references shows a chromatography medium/matrix/resin and various buffers (e.g. equilibration, loading, elution, and/or regeneration buffers), provision of these in a kit would have been obvious. It has been stated supra that each of the primary references shows a chromatography medium/matrix/resin that has a structure consistent with the limits of claim 2; therefore claim 10, which parallels claim 2, would have been obvious.

In this rejection, no weight is given to the intended use of the kit, according to any instructions provided. Instructions are merely printed matter and cannot distinguish over the prior art. In re Nagai 70 USPQ2 1862.

Claim 9 is rejected under 35 U.S.C. 103(a) as being unpatentable over Lowe et al in view of Hunt et al (US 2002/0110495, cited on Form 892).

The Lowe et al reference has been cited supra, against claim 1 for showing chromatographic separation of antibodies/immunoglobulins on a multi-modal chromatography medium/matrix resin, which is consistent with that recited in instant claim 1. Hunt et al show that it was known to provide a chromatography medium/matrix/resin, in a kit, along with buffers. The chromatography medium/matrix/resin provided in the kit can be any one of a variety of types, including an ion exchange resin. Since the primary reference shows a chromatography medium/matrix/resin and various buffers (e.g. equilibration, loading, elution, and/or regeneration buffers), provision of these in a kit would have been obvious.

In this rejection, no weight is given to the intended use of the kit, according to any instructions provided, in accord with *In re Nagai* 70 USPQ2 1862.

DOUBLE PATENTING

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422

Art Unit: 1644

F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-3 and 7-10 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-3, 17, 19-22 and 27-29 of copending Application No. 10/589,717. Although the conflicting claims are not identical, they are not patentably distinct from each other, because the instant and copending method claims clearly pertain to common embodiments, for the case in which antibody is adsorbed to the multi-modal chromatography resin. The instant and copending kit claims are related as a subcombination and a combination (a "second chromatography column" added to the subcombination of the instant claims provides for the combination of the copending claims); in this consideration of the obviousness of copending claims over one another, no weight is given to the intended use of the kit, according to any instructions provided.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Art Unit: 1644

CONTACTS

Any inquiry concerning this communication from the examiner should be directed to David A. Saunders, whose telephone number is 571-272-0849. The examiner can normally be reached on Mon.-Thu. from 8:00 am to 5:30 pm and on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan, can be reached on 571-272-0841. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Typed 11/9/07 DAS

A handwritten signature in black ink, reading "David A. Saunders". The signature is fluid and cursive, with a long horizontal line extending from the end.

DAVID A. SAUNDERS
PRIMARY EXAMINER